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ST. MICHAEL'S HOSPITAL
A teaching hospital affiliated with the University of Toronto

LETTER OF INFORMATION AND CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Before agreeing to take part in this research study, it is important that you read the information in this research consent form. It includes details we think you need to know in order to decide if you wish to take part in the study. If you have any questions, ask a study doctor or study staff. You should not sign this form until you are sure you understand the information. All research is voluntary. You may also wish to discuss the study with your family doctor, a family member or close friend. If you decide to take part in the study, it is important that you are completely truthful about your health history and any medications you are taking. This will help prevent unnecessary harm to you.

Title of Research Study:
Cardiovascular Toxicity of Concentrated Ambient Fine, Ultrafine and Coarse Particles in Controlled Human Exposures - Project #3 of the Particulate Matter Centers Studies

Study Short Title: PM Center Study

Investigator(s):
Principal Investigator:
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), Associate Professor
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223 College St. Toronto ON M5T 1R4
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Director of the Pulmonary Function Laboratory and Exercise Testing Laboratory
St. Michael's Hospital, 30 Bond Street, 6 – Bond, Suite 6045 Toronto, ON
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Physician supplying medical assistance at the Gage Occupational and Environmental Health Unit:
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Respirologist/Immunologist
Gage Occupational and Environmental Health Unit
223 College St. Toronto, ON
Phone (416) 978-5883 Monday to Friday, 9:00am to 5:00 pm.

Study Sponsor
The United States Environmental Protection Agency – National Center for Environmental ;earch

The study (project #3) is one of five projects included in the Harvard PM Center EPA grant to be carried out through collaborations with the Harvard School of Public Health

Purpose of the Research:

Current levels of air pollution are impacting public health. Air pollution is a mixture of gases and particles. Particles are made up of different chemical components and vary in size. The smaller a particle is, the deeper it can be inhaled into the lungs. It is important to examine the chemical components, sizes and sources of particles and health effects of pollutants in controlled environments to better understand how current air quality regulations should be changed, if at all. In this study you will be asked to breathe concentrated polluted air taken from right outside our facility on College Street, in Toronto. Using our controlled particle exposure facility, we can take the air from outside and concentrate it to make it the amount of pollution we want. We have done over 200 of these types of exposures on people. A new state-of-the-art human exposure facility being built at the University of Toronto, in collaboration with The Harvard School of Public Health, will now allow us to examine responses to different sizes of these particles: (a) fine; (b) ultrafine; and (c) coarse, in downtown Toronto. An exposure to (d)filtered air (no particles), will be done to compare what your regular responses might be.

Description of the Research:

You are invited to participate in this study for healthy, non-smokers aged 18-50 years, and attend the Gage Occupational and Environmental Health Unit for a total of nine visits. The first baseline visit will ensure eligibility into the study and familiarity with test procedures. During this visit, a health questionnaire will be completed, a medical examination will be carried out by one of the study physicians, a skin prick test, and a resting heart test (electrocardiogram, ECG) will be performed (tests detailed below). This baseline visit will be approximately three hours long. If you qualify to participate in this study, study visits will be arranged.

The four exposures each have two days of tests (8 days in total), with a minimum of 2 weeks between exposures. The exposures will be 2 hours in duration and will be delivered via a small facemask in controlled amounts. Each exposure involves coming to the Gage for about 6 hours on the exposure day, and for about 2 hours on the day after. The concentration of particles to be studied will be equal to the maximum levels that are sometimes found in the air in downtown Toronto and other cities The exposure to the different particle size concentrations and filtered air could be in any order, and you will not be told until after the study which exposure was 1^{st}, or 2^{nd}, 3^{rd} or 4^{th}. A medical doctor will be in attendance during all exposure visits. One month following the 4^{th} set of exposure visits, you will receive a follow-up phone call.

The tests that will be performed on the first baseline visit and/or throughout each of the four exposure visits will be the following:

Screening Visit Testing - one visit only needed

Tests (in order)	Definition/method	Time requirement	Purpose
1. Consent	Consent and information form read by you	As long as you need to fully understand what you are being asked to do	To obtain informed consent
2 Medical History/Exam	A physical exam and medical history to access health (Subjects must be healthy, non-smokers, 18-49 years of age, without cardiovascular disease, hypertension (BP>140/90 mm Hg) or diabetes, free of lipid medication use or inhaled/oral corticosteroids and free of respiratory tract infections for at least three weeks prior to exposure testing)	Approximately 30 minutes	Health inclusion/exclusion criteria assessment by doctor
3 Pulmonary Function Testing (Spirometry)	Breathing tests This involves taking a deep breath and then blowing all the air out as fast and hard as possible	5 to 15 minutes	To confirm normal lung function
4 electrocardiogram, or heart test	Standard 12 lead ECG Sticky electrodes will be placed on your chest and wires attached to an electrocardiogram (ECG) machine.	20 minutes	to confirm heart function normal
5 Skin prick testing for common allergens	A drop of diluted extract from each of 15 common inhaled allergens, such as grass pollen and ragweed, will be applied to the skin on the underside of the forearm, along with a drop of saline (baseline control) and a drop of 1% histamine (positive control). Then, at each drop, a small prick will be made with the tip of a needle. If there is a positive reaction, a small raised reddened area with a surrounding flush will occur within 10 min at the drop(s), but will start to disappear after 10-20 min	20 minutes	This is done to see if you have any allergies that might affect your nose or breathing, and could confuse your test results.
6 Blood test	A sample of blood will be taken from your arm with a small needle (about 2 teaspoons)	1 minute	To confirm blood sugar, cholesterol normal

Exposure Visits Testing - 4 exposure visits (each has an exposure day, and a visit 24 hours post exposure)

Test	Definition/method	Time	Frequency
1.Spirometry	A set of simple, routine **breathing tests** will be performed. This involves taking a deep breath and then blowing all the air out as fast and hard as possible, to show if there are any changes to lung function because of exposure to the pollution.	From 5 to 15 minutes	throughout exposure day visits
2.Blood taking	**A sample of blood** of about 40 mls (three tablespoons) will be taken from the arm to measure how well the blood clots, to look at inflammatory measures. The sample will be taken from a vein in the arm with a needle.	Approx. 2 minutes	Before, after and 24 hours after exposure
3.Ultrasound	To measure **blood flow in the arm**, you will be asked to lie on your back on an examining table and rest for 10 minutes. A baseline blood pressure will be taken, then a baseline ultrasound measurement will be taken by placing an ultrasound device on the right upper arm. This instrument measures blood flow using high frequency sound that cannot be heard or felt. Next, a blood pressure cuff will be placed on the right upper arm and inflated at a pressure of 200 millimetres mercury for four minutes (This is about the same pressure that the cuff is inflated to during a standard blood pressure measure, but for longer). After the four minutes, the cuff will be deflated, and blood flow measures in the arm will be taken over the following two minutes using the ultrasound device that the technician will hold in their hand. If your baseline blood pressure was not less than 100/50, **a 0.4 mg nitroglycerin pill** will be given to take under the tongue. Nitroglycerin pills are used by doctors when they want the patient's blood flow to be less constricted, as in the case of heart disease. It dilates the blood vessels, and this can cause your blood pressure to decrease, and make you feel dizzy, so that is why it is not given to you if your blood pressure is already low. 3 min later an ultrasound measurement will be taken on the right upper arm. This is a standard part of the test and is used to tell if any changes in blood flow are caused by changes in smooth muscle that surround the blood vessel or changes in the cells that line the inside of the blood vessel. A minor or major headache may develop after taking the nitroglycerin, although it may be limited in duration and will resolve in minutes to hours. When your blood pressure is the same as what it was at the beginning of the test, (usually after 2-10 minutes), you will be allowed to sit up.	45 minutes	Before after and 24 hours after exposure

4.Ambient CAP exposure	Controlled exposure of **concentrated ambient particles**, as well as a control exposure session with filtered air	2 hours	Exposure day
5. Questionnaire	You will be asked to complete a **questionnaire** about the symptoms you experience (if any) during and following the exposures.	5 minutes	Pre post exposure
6.ECG/Holter	You will be connected to an electrocardiogram (ECG) machine to monitor heart throughout exposure. Sticky electrodes will be placed on your chest and wires attached. This will also monitor your heart rate.	monitor thru exposure	Exposure day
7. Capnography	To measure the **concentration of carbon dioxide** (CO_2) during normal breathing, you will be asked to insert the two nasal prongs of a CO_2 sample line just inside the nostrils and to breathe normally through the nose for 5 minutes while resting quietly. Immediately following the CO_2 test, the breathing rate (# of breaths/minute) and volume (litres of air exhaled/minute) will be measured. This involves placing a paper tube in the mouth and breathing normally for 1-3 minutes with a nose clip on. These two tests will be done immediately before the exposure, at the start and every 30 minutes during exposure, at the end of the exposure day, and the next day upon arrival. A sample of blood taken by **finger prick** will be done once only, during the initial screening visit. Less than 1 ml (less than ¼ teaspoon) will be collected into thin glass rods from a small pin prick on one finger. This will let us compare the amount of CO2 in your blood with the amount you breath out of your lungs.	5 minutes	Pre, post and during exposure
8.Echo-cardiography	To examine vascular function (blood flow) An **echo-cardiograph** will be taken. This involves lying on your side and placing an ultrasound probe on your chest between your ribs to get a picture of your heart. You may feel some pressure when the probe is pushed slightly against your chest.	15 minutes	Pre, post and 24 hrs post exposure
9.Finometer	Non-invasive beat to beat finger arterial blood pressure and hemodynamic monitor Measurements relating to blood pressure will also be measured with a **Finometer**, that attaches to the finger with a little cuff.	During exposure	Exposure day
10.Blood pressure	**Blood pressure** will be measured with an automated arm cuff, as during a physical exam with a family doctor.	5 minutes	Pre, during and post exposure

Potential Harms (Injury, Discomforts or Inconvenience):

Nitroglycerine Pill: A minor or even a major headache may develop after taking the nitroglycerin pill, although it may be limited in duration and will resolve in minutes to hours. The nitroglycerine pill will cause the blood vessels to open up more, and this will cause a lowering of the blood pressure. Lightheadedness because of a lowering of blood pressure often occurs, but you will be lying down until your blood pressure returns to normal, and all feelings if any, of faintness pass, approximately 10 minutes.

Blood Collection: There may be a small amount of bleeding when blood is taken from the vein and there may be slight discomfort and bruising or redness that will usually disappear in a few days. The finger prick test may cause slight discomfort and may leave a little mark that will disappear within a few days.

Skin-Prick Test: There may be a slight discomfort during the skin-prick with the needle, and possible redness and itching at the skin-prick(s) from the allergen(s).

Particle Exposure: Exposure to high concentrations of particles from ambient air has been reported to result in cough, shortness of breath, chest discomfort or headache. The development of a cold a few days after the exposure is also possible, but not likely. No permanent health effects, and no cumulative effects have been reported from short-term exposures to particles at the concentrations used in this study.

Spirometry: Shortness of breath or cough sometimes occurs after the test. If this does occur, breathing should return to normal within minutes.

Electrocardiogram (ECG): There is a slight irritation when the electrodes are removed from the chest and possible redness of the skin.

Carbon dioxide test: A slight discomfort (tickle) in the nostrils when the nasal prongs are inserted.

Breathing rate & volume test: A slight dryness in the throat and a slight discomfort from the nose clip.

Blood Pressure: There is a slight discomfort while the pressure cuff is inflated.

Reproductive Risks:

Women are strongly advised to avoid becoming pregnant and/or breast-feed because of the possible unknown effects on the fetus. The participant should be advised to tell the investigator immediately if she thinks she may have become pregnant during the study, and you should be aware that you will be withdrawn from the study because of these unknown risks. Current research does not show any male reproductive risks associated

with inhalation of pollutants, nor any female reproductive risks with these concentrations of air pollutants.

Potential Benefits: The data collected will add to the previous exposure studies data and potentially be used to modify the current air quality standards. No direct benefit will result from participating in the research study. The study physician will contact by telephone your family doctor, and suggest follow-up of any significant abnormal test results discovered during baseline tests and physical exam only with your permission.

Treatment Options: This is not a treatment. Participation in research is voluntary. You are under no obligation to participate.

Confidentiality and Privacy: Confidentiality will be respected and no information that discloses your identity will be released or published without your consent unless required by law. This consent form is to be retained at the Gage Occupational and Environmental Health Unit. The research records may be viewed by the Research Ethics Board of St. Michael's Hospital as well as for monitoring purposes by the coordinating centre (Environmental Protection Agency – National Center for Environmental Research), but your name will not be associated with any results.

lication of Results: If the results of this study are published, presented at ferences, seminars or other public forums, the data will not indicate your identity in any way. It is possible that the investigators may choose not to publish and may only use the results to inform further studies.

Reimbursement: You will be paid $300.00 for the entire study for reasonable out-of-pocket expenses e.g. time commitment to do the study, transportation costs, etc. If you withdraw from the study prematurely, you will be reimbursed at the current Ontario Ministry of Labour approved minimum hourly rate for time prior to withdrawal.

Compensation for Injury: If you suffer a physical injury as a direct result of the administration of study procedures, medical care may be obtained in the same manner as ordinarily obtained in any other medical treatment. In no way does signing this form waive your legal rights nor relieve the investigators, sponsors or involved institutions from their legal and professional responsibilities.

Participation and Withdrawal: Participation in research is voluntary. If you choose not to participate, you will continue to have access to customary care at St. Michael's Hospital. If you choose to participate in this study you can withdraw at any time without any effect on the care they will receive at St. Michael's Hospital's. If you are a student, your status as a student will not be affected in any way by choosing to participate or not participate.

Your withdrawal from the study does not necessarily include the withdrawal of any data compiled up to that point. Upon completion of the research (your last study day), you will be asked if you would like a copy of the publications resulting, and if so they would be picked up at a later date or sent by mail.

Research Ethics Board Contact: If you have questions as a research participant, please contact Dr. J. Spence, Chair of the Research Ethics Board (416) 864-6060 ext. 2557.

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I acknowledge that the research study described above has been explained to me and that any questions that I have asked have been answered to my satisfaction. I have been informed of the alternatives to participation in this study, including the right not to participate and the right to withdraw without compromising the quality of medical care at St. Michael's Hospital for me and for other members of my family. As well, the potential risks, harms and discomforts have been explained to me and I also understand the benefits (if any) of participating in the research study.

I understand that I have not waived my legal rights nor released the investigators, sponsors, or involved institutions from their legal and professional duties. I know that I may ask now, or in the future, any questions that I have about the study or the research procedures. I have been assured that records relating to me will be kept confidential and that no information will be released or printed that would disclose personal identity without my permission unless required by law. I have been given sufficient time to read and understand the above information.

I hereby consent to participate, and will be given a signed copy of this consent form.

Participant's Name: (please print) _____

Date: _____ Participant's Signature: _____

Person obtaining Consent: (please print) _____

Position: _____

Date: _____ Signature: _____